Translation

PCT/JP2003/013152

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

08 APR 2005

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 663991	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP2003/013152	International filing date (*day/month/year*) 15 October 2003 (15.10.2003)	Priority date (*day/month/year*) 16 October 2002 (16.10.2002)
International Patent Classification (IPC) or national classification and IPC A61K 31/4439, 47/02, 9/16, 9/28, 9/48, A61P 1/04		
Applicant TAKEDA CHEMICAL INDUSTRIES, LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19 November 2003 (19.11.2003)	01 July 2004 (01.07.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

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International application No.
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I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

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IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☒ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

See supplemental sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☒ all parts.

☐ the parts relating to claims Nos. _____ .

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV. 3.

The invention set forth in claims 1-20 pertains to "a stable solid preparation containing a non-toxic base and an amorphous benzimidazole compound having a proton pump inhibitor (PPI) function."

The invention set forth in claims 21 and 22 pertains to "a process for producing a stable solid preparation containing an amorphous benzimidazole compound having a PPI function characterised by employing a specific package form."

The invention set forth in claims 23-26 relates to "a process for producing an optically active amorphous lansoprazole (R-compound) characterised by the inclusion of a specific step."

These groups of inventions are not considered to be one invention only or a group of inventions so linked as to form a single general inventive concept.

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-26	YES
	Claims		NO
Inventive step (IS)	Claims	23-26	YES
	Claims	1-22	NO
Industrial applicability (IA)	Claims	1-26	YES
	Claims		NO

2. Citations and explanations

Documents

Document 1: EP 423748 A (Takeda Chemical Industries, Inc.), 24 April 1991

Document 2: EP 496437 A2 (Aktlebolaget Hassle), 29 July 1992

Document 3: EP 1004305 A1 (Eisai Co., Ltd.), 31 May 2000

Document 4: EP 248634 A2 (Nippon Chemiphar Co., Ltd.), 9 December 1987

Document 5: JP 2001-39975 A (Eisai Co., Ltd.), 13 February 2001

Document 6: EP 224249 A1 (Syntex (USA) Inc.), 3 June 1987

Document 7: WO 00/78745 A2 (Takeda Chemical Industries, Ltd.), 28 December 2000

Document 8: EP 1191025 A1 (Takeda Chemical Industries, Ltd.), 27 March 2002

Document 9: JP 11-322605 A (Polar Chemical Industries, Inc.)

Explanations

1. The invention set forth in claims 1 and 8-9 does not involve an inventive step in the light of documents 1-6.

Documents 1-3 disclose preparations comprising benzimidazole compounds such as lansoprazole (document 3)

and basic inorganic salts such as those of magnesium carbonate (documents 1-2), magnesium hydroxide (documents 1-2) and sodium carbonate (documents 2-3) as a stabilised preparation.

Moreover, document 4 (claims 14-23) discloses a preparation comprising benzimidazole compounds and a basic substance as a stabilised preparation.

The invention set forth in claims 1 and 8-9 differs from those disclosed in documents 1-4 in terms of the benzimidazole compounds being amorphous.

However, document 5 indicates that sulfoxide derivatives of benzimidazole compounds such as rabeprazole, lansoprazole and the like have conventionally been prepared as amorphous or amorphous solids (powder). Therefore, it would be easy for a person skilled in the art to prepare the benzimidazole compounds in documents 1-4 using the amorphous form.

Furthermore, document 4 (table 1) indicates that amorphous benzimidazole compounds are stable and document 6 (abstract) indicates that the solubility and efficiency of amorphous benzimidazole compounds are greater than the crystalline form. Therefore, it would be easy for a person skilled in the art to use the amorphous form of the benzimidazole compounds in documents 1-4.

2. The invention set forth in claims 1-9 does not involve an inventive step in the light of documents 1-4 and 7-8.

The invention set forth in claims 1-9 of the present application differs from those disclosed in documents 1-4 in terms of the benzimidazole compounds containing amorphous lansoprazole of an R-compound or S-compound and being an optically active amorphous substance.

However, amorphous benzimidazole compounds of an optically active substance, such as amorphous lansoprazole of an R-compound (+) or S-compound (-), which are

presented in documents 7 and 8, are known and it would be easy for a person skilled in the art to prepare a preparation using an optically active substance in amorphous form containing amorphous lansoprazole of an R-compound or an S-compound as the benzimidazole compounds in documents 1-4.

3. The invention set forth in claims 10-13 and 19-20 does not involve an inventive step in the light of documents 1-8.

Document 1 (page 8, lines 34-35) indicates that tablets and the like are coated with an enteric and sustained-release control layer.

Furthermore, a person skilled in the art would be able to provide an intermediate coating layer according to necessity.

4. The invention set forth in claims 14-18 does not involve an inventive step in the light of documents 1-8.

It would be easy for a person skilled in the art to use two or more types of the basic inorganic salts presented in documents 1-4 according to necessity.

In addition, the invention set forth in claims 14-18 does not exhibit any particular effect that could not be expected from documents 1-8.

5. The invention set forth in claims 21-22 does not involve an inventive step in the light of documents 1-9. Nitrogen gas replacement packaging and packaging that uses a deoxidiser are known as means for stabilising preparations, as disclosed in, for example, document 9.

6. The invention set forth in claims 23-26 is novel and involves an inventive step.

None of the documents cited in the international

search report discloses or suggests a method for producing an amorphous lansoprazole optically active material characterised in that the hydrated crystals of the lansoprazole optically active material are maintained at 20-100°C.

7. The inventions set forth in claims 1-27 are industrially applicable.